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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,920	04/20/2007	Lin Zhi	119378-00314 / 1110US	3750

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EXAMINER	
THOMAS, TIMOTHY P	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
08/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,920	ZHI ET AL.	
	Examiner	Art Unit	
	TIMOTHY P. THOMAS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52,54-84,86-136 and 138* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-10,12-18,25-28,30-34,36,46,99,107,108,120,126,128,130,131 and 138* is/are rejected.

7)☒ Claim(s) *36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/22/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 5,11,19-24,29,35,37-45,47-52,54-84,86-98,100-106,109-119,121-125,127 and 132-136.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-52, 54-84, 86-120, 126-131 and 138 in the reply filed on 6/3/2008 is acknowledged. The traversal is on the ground(s) that instant claim 1 excludes the compound identified in the Coghlan reference used for making the Lack of Unity determination, by the proviso wherein at least one position selected from among R_2, R_3, R_4, R_5, and R_6 is not hydrogen. This is not found persuasive because the structure in common of the compounds within the Markush group of claim 1 (also the feature in common with other groups) is only the core structure of Formula I (each of the three R_1 substituents of Formula I are different); therefore the common technical feature linking the inventions is a compound that contains the core structure of formula I. Since the compound identified in Coghlan has this core structure (even though the compound does not anticipate claim 1), the technical feature has been taught in the prior art, the technical feature is not "special" and therefore the inventions are not so linked by the same or a corresponding special technical feature as to comprise a single general inventive concept.

The requirement is still deemed proper and is therefore made FINAL.

2. Applicant's election without traverse of the compound (Z)-5-(2'-fluoro-3'-methyl-benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]-quinoline (compound 28; the compound of Formula I where R_1 is Formula II, R_2 is F, R_3 is CH_3, and R_4-R_6 are each H), with the identification that claims 1-4, 6-10, 12-18, 25-

28, 30-34, 36, 46, 99, 107, 108, 120-126, 128, 130-136 and 138 read on the elected specie in the reply filed on 6/3/2008 is acknowledged.

3. Claims 121-125 and 132-136 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 6/3/2008.

4. Claims 5, 11, 19-24, 29, 35, 37-45, 47-52, 54-84, 86-98, 100-106, 109-119, 127 and 129 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/3/2008.

Oath/Declaration

5. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because:
> It does not identify the mailing address of each inventor. A mailing address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing address should include the ZIP Code designation. The mailing address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.

Specification

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: 1,2-Dihydro-9-hydroxy-10-methoxy-1,2,4-trimethyl-5H-chromeno[3,4-f]quinoline Compounds that Modulate Glucocorticoid Receptors.

Claim Objections

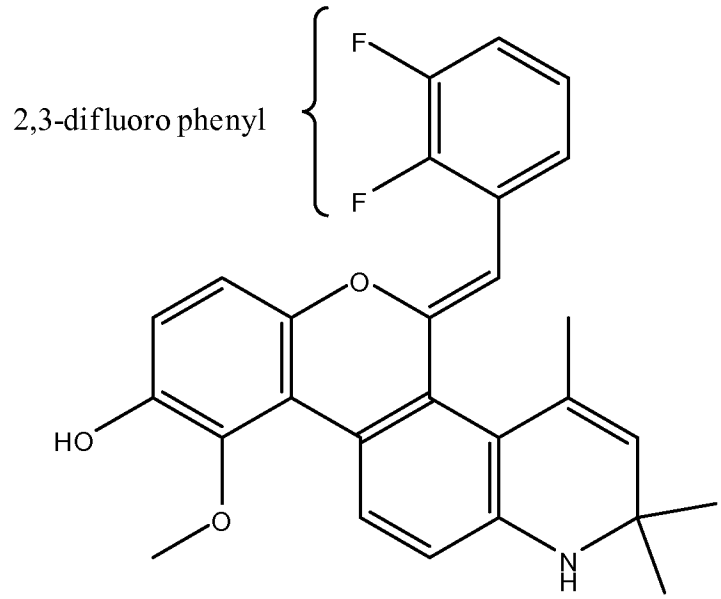
7. Claim 36 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 36 recites the exclusion of a compound where all of R_2-R_6 are H; this exclusion is already present in claim 1 (p. 6, lines 1-2); therefore claim 36 does not further limit the subject matter of claim 1, on which it depends.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-4, 6-10, 12-18, 25-28, 30-34, 36, 46, 120, 126, 128, 130-131 and 138 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For example, it is not clear whether the following compound, taught by Coghlan et al. (WO 02/02565 A2; 2002; IDS reference BA; p. 230, Example 373) is within or excluded by the claim subject matter:



The exclusion phrase of the last two lines of claim 1 would exclude this compound from the compounds of Formula I; however, this compound would also be a "derivative" of the elected compound (substitution of the 3 fluoro for a 3-methyl gives the elected compound). Since it is not clear whether the exclusion phrases apply to derivatives, it is not clear whether this compound is in the metes and bounds of or excluded from the subject matter of the instant claims.

It is not clear whether the excluded compounds of lines 1-9 of p. 6 in claim 1 are applicable only to the compounds of Formula I , or whether the exclusions also apply to the undefined "derivatives" of a compound of Formula I. For example,

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-4, 6-10, 12-18, 25-28, 30-34, 36, 46, 120, 126, 128, 130-131 and 138 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written

description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1extends the compounds of the instant claims to “derivatives” of a compound of formula I. While it is acknowledged that the application has provided written description of formula I compounds, the description does not extend beyond formula I compounds to demonstrate applicant was in possession of the much broader genus of "derivatives" of formula I compounds, including “derivatives” of the elected compound at the time of filing.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> “To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that “the inventor invented the claimed invention.” Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (“[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.”). Thus, an applicant complies with the written description requirement “by describing the invention, with all its claimed limitations, not that which makes it obvious,” and by using “such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.” Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.” Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus …") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation

between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to a compound of Formula I or a pharmaceutically acceptable derivative thereof

(1) Level of skill and knowledge in the art:

The level of skill and knowledge in the art are high

(2) Partial structure:

Formula I has been disclosed and claimed. Hundreds of compounds that have the structure of Formula I have also been disclosed and claimed. No other derivatives, outside of these compound of Formula I, have been disclosed

(3) Physical and/or chemical properties and (4) Functional characteristics:

The compounds are glucocorticoid receptor modulators.

(5) Method of making the claimed invention:

No method of making any derivative outside of compounds of Formula I have been disclosed.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1-4, 6-10, 12-18, 25-28, 30-34, 36, 46, 120, 126, 128, 130-131 and 138 is/are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are limitless to any "derivative" of the elected compound. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of compounds of Formula I, where R_1 is selected from Formula II, III, or IV, and compounds identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-4, 6-10, 12-18, 25-28, 30-34, 36, 46, 120, 126, 128, 130-131 and 138 are rejected under 35 U.S.C. 102(b) as being anticipated by Coghlan et al. (WO 02/02565 A2; 2002; IDS reference BA).

This rejection is based on construing claim 1 in the broadest reasonable terms, where the exclusion of the last two lines of claim 1 applies to a compound of Formula I, but not to a "derivative" of a compound of Formula I. The following compound would be both a derivative of the elected compound and an excluded compound of Formula I, and as a derivative of the elected compound is within the metes and bounds of the instant claims. Coghlan teaches a compound with the same core structure of Formula I as the elected compound, where R_1 is Formula II and R_2 and R_3 are both F, and R_4-R_6 are each H (2,3-difluoro “derivative” of the elected compound; p. 230, Example 373); compounds are useful as glucocortiocoid-selective anti-inflammatory agents (title); pharmaceutical compositions that comprise a compound and a pharmaceutically acceptable carrier (p. 59, lines 1-3). The compound would be expected to have the

same activity as the elected compound, due to the very similar structure, as recited in claims 126, 128, 130 and 131.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

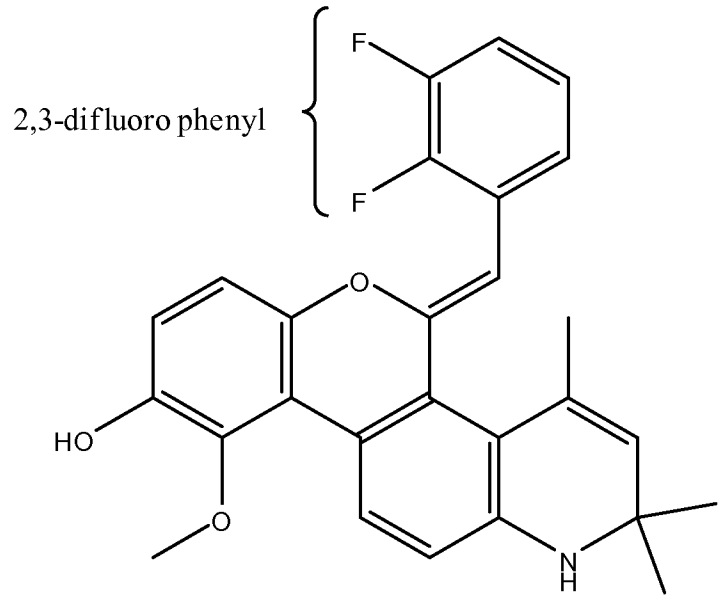
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

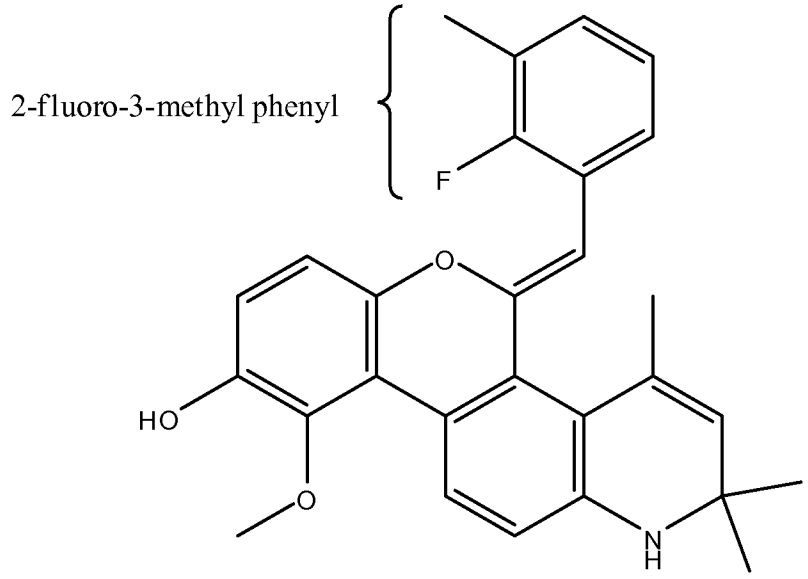
17. Claims 1-4, 6-10, 12-18, 25-28, 30-34, 36, 46, 99, 107-108, 120, 126, 128, 130-131 and 138 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coghlan et al. (WO 02/02565 A2; 2002; IDS reference BA) and Patani et al. ("Bioisosterism: A Rational Approach in Drug Design"; 1996; Chem. Rev.; 96:3147-3176).

Coghlan teaches a compound with the same core structure of Formula I, where R_1 is Formula II and R_2 and R_3 are both F, and R_4-R_6 are each H (2,3-difluoro analog of the elected compound; p. 230, Example 373); compounds are useful as glucocortiocoid-selective anti-inflammatory agents (title); pharmaceutical compositions that comprise a compound and a pharmaceutically acceptable carrier (p. 59, lines 1-3). Coghlan does not teach the elected compound. Patani teaches bioisosteres that elicit similar biological activity, due to common physicochemical properties of the bioisosteres (p. 3148, 2nd paragraph; bioisosteric replacements include methyl group for fluoro (p. 3148, Table 2). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the 2,3-difluoro compound of Coghlan Example 373 by substituting a methyl group for the F at the 3 phenyl position, which would have given the elected compound, as depicted by the structures:

Coghlan 2,3-difluoro compound of Example 373:



Elected Compound:



The motivation to modify the compound would have been the similar activity expected for the bioisosteric substitution of methyl group for the fluoro atom, as taught by Patani. The properties recited in claims 126, 128 and 130 would be possessed by the same compound made as in the elected compound of the instant claims.

Conclusion

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571)272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy P Thomas/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614